

# Evaluation of Consequences of Dust Positioned in Southwest of Iran on Coagulant Factors

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## Abstract

**Background:** Various regions in Iran, especially the Khuzestan Province, have been covered by dust and dirt during the past two years due to environmental changes in the Middle East. We sought to evaluate the effect of these pollutants on the coagulant factors of people residing in Abadan and Khoramshahr, two major cities of Khuzestan Province.

**Methods:** One hundred twenty-nine healthy individuals were enrolled into this study, and their prothrombin time as well as fibrinogen, platelet, and Factor VIII levels were measured before and after climate changes.

**Results:** After climate changes, the mean prothrombin time decreased, while the fibrinogen, platelet, and Factor VIII levels rose.

**Conclusion:** The results of this study suggest that the pollutants deployed in the Middle East can affect prothrombin time as well as fibrinogen, platelet, and Factor VII levels considerably and increase coagulant state. The pollutants can, consequently, increase the risk of cardiovascular diseases. It seems that cooperation at government levels between Iran and its neighboring countries is required to reverse desertification and avoid inaccurate usage of subterranean water resources so as to lessen air pollution.

Please cite this article as: Saeb K, Sarizade GhR, Khodadi M, Biazar E. Evaluation of Consequences of Dust Positioned in Southwest of Iran on Coagulant Factors. *Iran J Med Sci.* 2013;38(2): 84-88.

**Keywords** • Air pollution • Prothrombin time • Middle East

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Received: 19 January 2012

Revised: 3 March 2012

Accepted: 22 April 2012

## Introduction

Over the past two decades, a growing body of evidence has led to a heightened concern about the potential deleterious health effects of ambient air pollution and its relation to cardiovascular diseases.<sup>1,2</sup> Several air pollutants have been associated with increased hospitalization and mortality as a result of cardiovascular diseases and stroke.<sup>1-9</sup> Based on the World Health Organization (WHO.) reports, annually more than 3,000,000 premature deaths occur all over the world, especially in under-developed countries, due to air pollution.<sup>10</sup> Previously, many authors noted that exposure to air pollution can activate inflammatory pathways, produce reactive oxygen species, lead to endothelial injury and dysfunction and thus arterial vasoconstriction, and effect alterations in blood coagulation factors. Thus far, the exact underlying mechanisms linking air pollutants to increased cardiovascular risk has remained unclear.<sup>2,11-13</sup> Recently, the American Heart Association (AHA) published a statement on the importance of air pollution in the development of cardiovascular diseases. One

of the potential biological mechanisms linking air pollution to cardiovascular diseases in the AHA statement involves indirect effects mediated through pulmonary inflammation and oxidative stress, which develop into a systemic inflammatory response.<sup>1</sup> Several studies have shown that aside from respiratory disorders, allergies, and cancers, little particles (less than 10 PM) in the air can decrease coagulation time and consequently increase the risk of cardiovascular diseases. These studies have primarily focused on the effect of pollutants from gasoline, petroleum, coal, and other fossil energy sources; be that as it may, little attention has been paid to the consequences of dust and sand on coagulant factors.<sup>14</sup>

During the past two years, a substantial amount of dust and dirt originating from Iraqi and Saudi deserts and arid wastelands has blanketed large areas of the Middle East, not least in Iran.<sup>15</sup> The dust is mostly composed of clay (.01 PM) and silica (10 PM), but the particles might be combined with heavy metals. Due to the small size of these particles, they seem to be able to affect coagulation state via the activation of macrophage and increase of IL-6 in the lungs.<sup>15</sup> To the best of our knowledge, there were no previously published data on the effect of the dust and sand deployed in the past two years in the Middle East on coagulation state. We, therefore, sought to evaluate the hypothesis that these pollutants can influence coagulant factors and increase coagulation state.

## Materials and Methods

At the first stage of the present study (pilot study), 30 male volunteers (pilot study group) residing in Abadan and Khoramshahr, two major cities of the southwestern Iranian province of Khuzestan, were randomly enrolled into this study. None of the volunteers had cardiovascular, hematological, infectious, or major congenital diseases. Smokers and drug users were excluded from the study.

The first blood sample (8 milliliters) was taken from each subject when clear weather became stable for at least 48 hours in the area. All the samples were kept at 4°C and sent to the laboratory within 30 minutes after sampling

for further analysis. While two milliliters of each sample were combined with sodium citrate, ethylenediaminetetraacetic acid (EDTA) was added to the other 6 milliliters. The samples combined with EDTA were initially used for platelet count (using the cell counter) before they were kept at -30°C for further measurements. All the samples were thereafter centrifuged (Eppendorf Centrifuge 5720/R/RH, 3000 (RPM), Hamburg Germany) for 10 minutes using the 3000-round-per-minute setting to gain serum. The plasma combined with sodium citrate was used to assess prothrombin time (PT), thromboplastin time (PTT), and fibrin degradation products (fibrinogen), whereas the plasma combined with EDTA was used to measure the level of coagulant Factors II, VIII, and X.

All of the analyses were carried out once again when dust had been deployed for a minimum period of 48 hours over Abadan and Khoramshahr.

## Results

The analyses on the data from the pilot group are summarized in table 1.

These preliminary findings suggested that climate changes made significant differences only in PT as well as fibrinogen, platelet, and Factor VIII levels (table 1). In the next step of the study, 129 volunteers were enrolled into the study if they met the criteria, which were originally defined for the pilot group. PT in addition to fibrinogen, platelet, and Factor VIII levels were compared before and after climate changes by means of the mentioned methods.

In this study, the data are presented as mean±standard deviation (SD). The comparison between the means before and after climate changes was performed using the paired *t*-test. A P value less than .05 was considered statistically significant.

After climate changes and dust deployment in Abadan and Khoramshahr, the mean PT of the subjects significantly decreased, whilst the platelet count and fibrinogen and Factor VIII levels rose. The means of PT and platelet count as well as the means of the fibrinogen and Factor

**Table 1:** Analysis of coagulant factors, before and after climate changes in the pilot group

	Clear weather	Polluted Weather	P value
PT (prothrombin time)	12.56±0.62 (sec)	10.22±0.97 (sec)	<0.001
PTT (partial thromboplastin time)	29.86±2.89 (sec)	29.71±2.90 (sec)	0.07
Fibrinogen	157.9±23.44 mg/dl	158.70±23.32 mg/dl	0.001
PLT (platelet count)	223300.0±63746.8 (10 <sup>3</sup> /μl)	258300.0±64905.84 (10 <sup>3</sup> /μl)	<0.001
Factor II	96.83±9.082 mg/ml	96.89±9.105 mg/ml	0.76
Factor VIII	0.25±0.075 mg/ml	0.27±0.076 mg/ml	<0.001
Factor X	9.58±0.909 mg/ml	9.69±0.802 mg/ml	0.08

VIII levels in the clear weather and after climate changes are summarized in table 2.

**Discussion**

So far, various studies have been conducted by many authors to assess the effects of pollutants on the individual's health, particularly coagulation state. Most of these studies have investigated the impact of air pollutants caused by fossil fuels, and their findings support the notion that pollutants less than 10 PM in size can affect QT dispersion, stimulate the inflammatory processes in the lungs, activate macrophages, enhance the production of IL-6, and finally increase coagulation state.<sup>10,16,17</sup>

The results of our study suggest that the dust deployed in the Middle East, similar to other pollutants, can affect the coagulant factors in blood. In concordance with our findings, many authors have stated that air pollutants can reduce PT and increase platelet levels, fibrin degradation products, and Factor VII levels.<sup>16</sup> PT measures the formation of the fibrin clot through the activity of the extrinsic and common coagulation pathways, which involve the interaction between the tissue factor and activated Factor VII, in addition to Factor X, Factor V, prothrombin, and fibrinogen.<sup>18</sup> Our finding of a mildly shortened PT in association with high concentrations of pollutants less than 10 PM in size apparently reflects air pollution-related changes in blood coagulation. PT depends on the concentrations of factors in the extrinsic (Factor VII) and common pathways (Factor X, Factor V, Factor II, and fibrinogen) and is reduced in the presence of traces of thrombin or other activated factors that may be produced in hypercoagulable states.<sup>19</sup> Given the fact that the alterations in the levels of Factor II and Factor X were not significant in the pilot group and given the elevated level of Factor VIII after climate change, it seems that the air pollutants in our region affect the extrinsic, but not the common, pathway.

The results from experimental and epidemiological studies that have evaluated the plasma concentrations of coagulation factors in association with air pollution exposure are far from conclusive. Mutlu et al.<sup>15</sup> reported that air pollutants less than 10 micrometers in size can reduce PT but raise fibrinogen and Factor VIII levels. They also noted that PTT can decrease in

the presence of pollutants, whereas the levels of Factor II, Factor X, and IL-6 can increase. Seaton et al.<sup>14</sup> found that pollutants less than 10 PM in size can increase platelet and Factor VII levels. Despite the fact that comparable results have been published by many investigators, some authors have found no correlation between air pollutions and coagulant factors in blood. Vermylen and Hoylaerts,<sup>19</sup> reported that PT can reduce in the presence of air pollutants; nevertheless, they found no significant relation between air pollution and platelet count, fibrinogen level, and Factor VII level. Consistent with the results of some of the previous studies, we found an association between fibrinogen and the levels of air pollutants.<sup>16</sup> In addition, we examined, for the first time, the concentration and activity of natural anticoagulant proteins but found no consistent association with air pollution levels.

In contrast to the results of the Mutlu et al. study,<sup>15</sup> PTT had no correlation with exposure to air pollutants in our study. Previous studies have suggested that air pollutants alter blood coagulation through the induction of the tissue factor. Because air pollutants are known to elicit pulmonary and systemic inflammatory responses, perhaps pollution exposure increases the levels of mediators capable of inducing tissue factor expression, thereby generating a tendency to hypercoagulability.<sup>1,14-20</sup> The absence of a correlation between PTT and exposure to air pollutants in our study is consistent with the above-mentioned hypothesis. Moreover, in this study, we observed a rise in the level of platelet count after exposure to pollutants. Similar observations were reported by Poursafa et al.<sup>21</sup> in children and young adults residing in Isfahan, the second most polluted industrial city in Iran.

A previous analysis of the mixture of dust positioned in the southwest of Iran revealed that it contains heavy metals such as uranium, thorium, arsenic, lead, zinc, cobalt, iron, copper, and nickel.<sup>22</sup> Sangani et al.<sup>23</sup> reported that sulfated metals (except for nickel) can decrease coagulation time by affecting coagulant factors.

The present study is not without limitations. A limitation of this study is that ambient air pollution was used as a surrogate for personal exposure, which may have contributed to measurement inaccuracy. Such a measurement error would

**Table 2:** Analysis of coagulant factors, before and after climate changes in healthy men residing in Khoramshahr and Abadan

	Clear weather	Polluted Weather	P value
PT(prothrombin time)	12.54±0.631 (sec)	10.37±0.944 (sec)	<0.001
Fibrinogen	153.19±21.656 mg/dl	172.56±24.596 mg/dl	<0.001
PLT(platelet count)	219279.07±62453.98 (10 <sup>3</sup> /μl)	256170.54±64095.03 (10 <sup>3</sup> /μl)	<0.001
Factor VIII	0.2585±0.00646 mg/ml	0.2875±0.07632 mg/ml	<0.001

generally tend to bias estimates toward the null,<sup>24</sup> and may affect the results. Nonetheless, the result of drawing upon ambient measurements to estimate exposure is likely to be only a modest underestimation of pollution effects. In addition, due to some laboratory difficulties, the effect of pollutants on IL-6 was not investigated in this study. Many authors have reported the effect of pollutants on IL-6 and, as a result, coagulant state in their surveys. However, in regard to the other published data, it can be argued that we would have found a significant rise in IL-6 levels after climate change if we had measured it. We also did not assess the effect of these pollutants on cardiovascular diseases directly. A reduction in coagulation time can increase the risk of cardiovascular diseases. Ruckerl et al.<sup>25</sup> suggested that air pollutants can increase the occurrence of cardiovascular diseases by affecting coagulation state. These findings were subsequently borne out by Conlon et al.<sup>26</sup> It can, therefore, be concluded that dust and dirt positioned in the Middle East can increase the incidence of cardiovascular diseases.

Although we found a positive association between air pollutants and platelet count, we did not assess platelet activity and aggregation. Nonetheless, the rise in platelet count in relation to air pollutants may be an indicator of early hematologic and hemostatic changes due to air pollutants.<sup>22</sup> Rudez et al.<sup>27</sup> demonstrated a relationship between air pollution and increase in platelet aggregation and coagulation activity; the authors, however, did not observe any obvious consequences of pollutants on systemic inflammation.<sup>17</sup>

## Conclusion

The results of this study support the hypothesis that the air pollutants deployed in the Middle East in the past two years can significantly affect the level of coagulant factors. Given the fact that the dust and dirt originates chiefly from the deserts and arid wastelands of Iraq and Saudi Arabia, it is advisable that Iran more actively engage with its neighbors in order to reverse desertification and alter the inaccurate usage of subterranean water resources with a view to reducing the dust particles in the region.

**Conflict of Interest:** None declared.

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